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ON NICOTINE & TOBACCO



Tobacco Control  
Legal Consortium



September 29, 2015

Leslie Kux

Associate Commissioner for Policy  
U.S. Food and Drug Administration  
10903 New Hampshire Avenue  
Silver Spring, MD 20993

**Re: Nicotine Exposure Warnings and Child-Resistant Packaging for Liquid Nicotine, Nicotine-Containing E-Liquid(s), and Other Tobacco Products; Docket No. FDA-2015-N-1514**

Dear Ms. Kux:

On behalf of organizations dedicated to protecting children from the harm caused by tobacco products, we appreciate the opportunity to provide comments to the U.S. Food and Drug Administration (FDA) regarding the advanced notice of proposed rulemaking (ANPRM), “Nicotine Exposure Warnings and Child-Resistant Packaging for Liquid Nicotine, Nicotine-Containing E-Liquid(s), and Other Tobacco Products; Request for Comments,” published on July 1, 2015 (docket no. FDA-2015-N-1514).<sup>1</sup>

<sup>1</sup> 80 Fed. Reg. 37555-37559.

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## SUMMARY

Liquid nicotine is extremely toxic and poses an urgent—yet preventable—poisoning threat, particularly to young children. Child-resistant packaging and nicotine exposure warnings are urgently needed for liquid nicotine products, and as such our organizations strongly urge the FDA to quickly publish rulemaking to require these common-sense measures. The FDA has clear authority under the Family Smoking Prevention and Tobacco Control Act to do so and is, in fact, the only federal agency with the current legal authority to take such action. Poison control centers continue to field hundreds of calls per month related to e-cigarettes, and one child in the United States has tragically already died from a liquid nicotine exposure. The FDA has a duty to act now to prevent further harm to children related to liquid nicotine poisoning. In order for the FDA to protect children from unnecessary poisoning, injury, and death, the FDA must quickly publish final deeming rules to ensure that the FDA has jurisdiction over all tobacco products and quickly finalize a rulemaking requiring child-resistant packaging and nicotine exposure warnings for liquid nicotine.

The following comments specifically recommend that the FDA:

- as soon as possible, publish a proposed rule requiring:
  - child-resistant packaging for liquid nicotine containers that is consistent with existing standards established and overseen by the U.S. Consumer Product Safety Commission (CPSC); and
  - nicotine exposure warnings on liquid nicotine containers that specifically describe the risks to children, including injury and death;
- promptly publish a final rule to deem all tobacco products subject to the FDA's authority under the Tobacco Control Act;
- promptly publish a final rule requiring child-resistant packaging and nicotine exposure warnings for liquid nicotine containers;
- utilize its premarket review authorities to ensure that products that pose a poisoning risk carry child-resistant packaging and nicotine exposure warnings;
- not accord a lengthy compliance grace period to any newly deemed liquid nicotine products not sold in child-resistant packaging; and
- after requiring child-resistant packaging and nicotine exposure warnings for liquid nicotine products, consider other measures to reduce child poisoning risk related to tobacco products including requiring the use of graphic warning labels, providing for public education, making liquid nicotine containers less attractive to children, prohibiting the use of flavors attractive to children, limiting liquid nicotine quantity and concentration, protecting against unintentional inhalation exposure, and ensuring the safety of refillable e-cigarette devices.

## **I. LIQUID NICOTINE POISONING IS A PUBLIC HEALTH PROBLEM REQUIRING URGENT ACTION**

### **A. *Nicotine Is Extremely Toxic and Can Be Lethal to Young Children***

Nicotine poisoning poses an immediate and urgent threat to child health. Nicotine is extremely toxic and is not a benign substance. Exposure to nicotine in lower doses can cause vomiting, hypertension, tachycardia, vasoconstriction, headache, dizziness and abdominal pain.<sup>2,3</sup> At increased doses, blockade of the autonomic ganglia can occur, leading to hypotension, hyporeflexia, tachycardia, excessive salivation, and possible burning sensation in the mouth, throat, and stomach.<sup>4,5</sup> In cases of very high doses, nicotine can be fatal. In addition to systemic effects, dermal exposure can also cause skin irritation, redness, and possible allergic reactions.<sup>6</sup>

Given the tolerance to nicotine that develops among regular users, a wide range of doses have been shown to lead to acute toxicity. Toxic effects would likely be seen at lower doses among the nicotine naïve, such as children, than among established adult users of e-cigarettes and other tobacco products.<sup>7</sup> Nicotine is in fact lethal to small children at very small doses. The estimated median lethal dose (LD<sub>50</sub>)<sup>8</sup> of nicotine in humans is 1 to 13 mg per kg of body weight.<sup>9,10</sup> For comparison purposes, studies have shown that nicotine is more lethal in mice (LD<sub>50</sub>: 3.3 mg/kg<sup>11</sup>) than either potassium cyanide (LD<sub>50</sub>: 8.5 mg/kg<sup>12</sup>) or inorganic arsenic (LD<sub>50</sub>: 145 mg/kg<sup>13</sup>).

In liquid form, nicotine is especially dangerous because it can be easily absorbed into the body. In addition to being easily absorbable transmucosally in the mouth, nicotine is also highly absorbable through the skin. Studies conducted on nicotine replacement therapies show a high bioavailability of nicotine. These studies have shown nicotine to have a transdermal bioavailability of 68-98%, compared with a 53-55% oral bioavailability in gum, making it very

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<sup>2</sup> Kim JW and CR Baum. Liquid nicotine toxicity. *Pediatric Emergency Care*. July 2015, 31(7): 517-524.

<sup>3</sup> Nicotine: Systemic agent. Emergency Response Safety and Health Database. National Institute for Occupational Safety and Health. [http://www.cdc.gov/niosh/ershdb/emergencyresponsecard\\_29750028.html](http://www.cdc.gov/niosh/ershdb/emergencyresponsecard_29750028.html).

<sup>4</sup> Ibid.

<sup>5</sup> Kim JW and CR Baum. Liquid nicotine toxicity. *Pediatric Emergency Care*. July 2015, 31(7): 517-524.

<sup>6</sup> Nicotine: Systemic agent. Emergency Response Safety and Health Database. National Institute for Occupational Safety and Health. [http://www.cdc.gov/niosh/ershdb/emergencyresponsecard\\_29750028.html](http://www.cdc.gov/niosh/ershdb/emergencyresponsecard_29750028.html).

<sup>7</sup> Benowitz NL, et al. Prolonged absorption with development of tolerance to toxic effects after cutaneous exposure to nicotine. *Journal of Clinical Pharmacology & Therapeutics*. July 1987. 42(1); 119-120.

<sup>8</sup> LD<sub>50</sub> refers to the amount of material administered in a single dose that would cause the death of 50% of a given group (typically studies using rats or mice).

<sup>9</sup> Mayer B. How much nicotine kills a human? Tracing back the generally accepted lethal dose to dubious self-experiments in the nineteenth century. *Archive of Toxicology*. 2013. 88; 5-7.

<sup>10</sup> Bassett RA, Osterhoudt K, Brabazon T. Nicotine poisoning in an infant. *New England Journal of Medicine*. 2014. 370; 2249-2250.

<sup>11</sup> Centers for Disease Control and Prevention. National Institute for Occupational Safety and Health. Nicotine. Available at <http://www.cdc.gov/niosh/idlh/54115.html>.

<sup>12</sup> Centers for Disease Control and Prevention. National Institute for Occupational Safety and Health. Cyanides. Available at <http://www.cdc.gov/niosh/idlh/cyanides.html>

<sup>13</sup> Centers for Disease Control and Prevention. National Institute for Occupational Safety and Health. Arsenic. Available at <http://www.cdc.gov/niosh/idlh/7440382.html>

dangerous to children even if it only comes into contact with the skin.<sup>14</sup> Studies have shown children and young adults to be more susceptible to the effects of nicotine poisoning through transdermal absorption than adults.<sup>15</sup>

Nicotine-containing liquid solutions (herein referred to as liquid nicotine) are also sold in a highly concentrated form, with some products containing upwards of 36 mg of nicotine per ml of liquid.<sup>16,17</sup> At this concentration, a small 15 ml dropper bottle of liquid nicotine would contain 540 mg of nicotine. Given the estimated lethal dose range of nicotine, even at the high end of this range this small bottle would contain enough nicotine to kill four 10 kg children (10 kg is an average weight for a one-year-old child). Even a single teaspoon of liquid nicotine at this concentration could kill a small child, and a smaller dose could make a child extremely ill. (See Table 1 with estimated lethal doses of liquid nicotine in various concentrations for the mean, 10 kg one-year-old child, assuming a median lethal dose [LD<sub>50</sub>] of 1-13 mg/kg.)

Liquid nicotine can also be deadly for grown adolescents and adults, albeit at higher doses. For instance, less than two tablespoons (25.3 ml) of 36 mg/ml liquid nicotine (even at the more conservative LD<sub>50</sub> of 13 mg/kg) could be lethal to a 70 kg (154 lbs) individual. Sub-lethal doses could also cause severe illness and hospitalization in adults. (See Table 2)

**TABLE 1: Median Lethal Dose of Nicotine for 10 kg 1-Year-Old Child**

<i>Concentration of nicotine</i>	<i>Median lethal dose range (assuming LD<sub>50</sub> of 1-13 mg/kg)</i>	<i>Common units of lethal dose (assuming conservative LD<sub>50</sub> of 13 mg/kg)</i>
<b>18 mg/ml</b>	0.6-7.2 ml	1 ½ tsp (1.5 tsp)
<b>24 mg/ml</b>	0.4-5.4 ml	1 tsp (1.1 tsp)
<b>36 mg/ml</b>	0.3-3.6 ml	< 1 tsp (0.7 tsp)

<sup>14</sup> Nicotine Drug Monograph. AFHS DI. American Society of Health System Pharmacists. <http://www.drugs.com/monograph/nicotine.html>.

<sup>15</sup> McBride J et al. Green tobacco sickness. *Tobacco Control*. Sept. 1998. 7(3); 294-298.

<sup>16</sup> Schwarz E. Toxic liquid nicotine and the dangers of e-cigarettes. *Emergency Physicians Monthly*. 27 June 2014. <http://epmonthly.com/article/toxic-liquid-nicotine-and-the-dangers-of-e-cigarettes/>.

<sup>17</sup> Goniewicz, ML et al. (2012). Nicotine levels in electronic cigarettes. *Nicotine & Tobacco Research*. January 2013. 15(1); 158-166.

**TABLE 2: Median Lethal Dose of Nicotine for 70 kg Adolescent/Adult**

<b>Concentration of nicotine</b>	<b>Median lethal dose range (assuming LD<sub>50</sub> of 1-13 mg/kg)</b>	<b>Common units of lethal dose (assuming conservative LD<sub>50</sub> of 13 mg/kg)</b>
<b>18 mg/ml</b>	3.9-50.6 ml	3 ½ Tbsp (3.4 Tbsp)
<b>24 mg/ml</b>	2.9-37.9 ml	2 ½ Tbsp (2.6 Tbsp)
<b>36 mg/ml</b>	1.9-25.3 ml	< 2 Tbsp (1.7 Tbsp)

The lethality of liquid nicotine has tragically been demonstrated in children. Last December, a one-year-old toddler in New York became the first confirmed U.S. death related to an unintentional exposure to liquid nicotine.<sup>18</sup> There are also press reports of a 2013 child death in Israel.<sup>19</sup> Children have sadly acted as our “early warning” system on the dangers of liquid nicotine poisoning; urgent action is needed in order to prevent any more harm to children.

**B. E-Cigarettes and Liquid Nicotine Have Caused a Dramatic Rise in Calls to Poison Control Centers**

Concerns about the risk to young children posed by liquid nicotine are borne out by data showing that e-cigarettes and liquid nicotine have caused a substantial recent spike in calls to poison control centers, particularly related to exposures to young children under the age of five. The American Association of Poison Control Centers (AAPCC) reported that in 2014 there were over 3,700 calls to poison control centers referencing exposure to e-cigarettes and liquid nicotine.<sup>20</sup> This represents a nearly 150% increase over the number of cases in 2013.<sup>21</sup> AAPCC data also indicate that nearly 2,000 poisonings were reported from January through July 2015, indicating that liquid nicotine poisoning remains a significant danger for children.<sup>22</sup>

These numbers are unsurprising given the increase in popularity of e-cigarettes. A 2014 study performed by the Centers for Disease Control and Prevention (CDC) and Georgia State University indicated that between 2010 and 2013, adult use of e-cigarettes more than doubled,

<sup>18</sup> Mohney G. First child’s death from liquid nicotine reported as ‘vaping’ gains popularity. *ABC News*. 21 Dec. 2014. <http://abcnews.go.com/Health/child-death-liquid-nicotine-reported-vaping-gains-popularity/story?id=27563788>.

<sup>19</sup> Toddler who ingested nicotine drop from electric cigarette was niftar in Jerusalem hospital. *The Yeshiva World News*. 29 May 2015. <http://www.theyeshivaworld.com/news/headlines-breaking-stories/170198/toddler-who-ingested-nicotine-drop-from-electric-cigarette-was-niftar-in-jerusalem-hospital.html>.

<sup>20</sup> Electronic cigarettes and liquid nicotine data. American Association of Poison Control Centers. Accessed 13 August 2015. [https://aapcc.s3.amazonaws.com/files/library/E-cig\\_Nicotine\\_Web\\_Data\\_through\\_7.2015.pdf](https://aapcc.s3.amazonaws.com/files/library/E-cig_Nicotine_Web_Data_through_7.2015.pdf).

<sup>21</sup> There were 1,543 calls to poison control centers in 2013.

<sup>22</sup> E-cigarette devices and liquid nicotine. American Association of Poison Control Centers. Accessed 13 August 2015. <http://www.aapcc.org/alerts/e-cigarettes/>.

with significant increases among current and former smokers.<sup>23</sup> This growth in popularity is not restricted to adult users, as alarming increases in e-cigarette popularity have been reported among middle and high school students. One survey indicated that 13.4% of high school students were regular e-cigarette users in 2014, up from only 1.5% in 2011.<sup>24</sup> As e-cigarettes continue to grow in popularity, the liquid nicotine used to refill these products is quickly becoming a common household product that is exposing more and more children to the dangers of nicotine poisoning. Further, a recent study indicated that 36% of e-cigarette users did not take additional safeguards to protect their children from liquid nicotine exposure by utilizing child-resistant caps or locking up bottles of liquid nicotine in containers inaccessible to children, and that 13% of users reported storing liquid nicotine on an open counter.<sup>25</sup> Alarmingly, 3% of those surveyed in the same study indicated that their child had attempted to drink liquid nicotine stored in accessible locations.<sup>26</sup> Without the immediate implementation of appropriate safeguards for these products, such as child-resistant packaging and nicotine exposure warnings, the number of children poisoned by liquid nicotine will continue to rise.

### **C. Liquid Nicotine Products Are Attractive to Children**

Liquid nicotine is a likely candidate for exposure to young children. It comes in a variety of containers, including glass and plastic dropper bottles similar in design to containers used to store many common household products. The use of such common containers can easily confuse children, who are unable to distinguish between harmful and benign substances stored in these containers. These risks are exacerbated by the eye-catching labeling of these containers. Liquid nicotine is marketed using brightly colored labels that contain cartoons, depictions of fruit and candy, and even symbols and images of popular food products marketed to children, such as “Captain Crunch” or “Gummy Bears” (see Appendix A). The liquid itself is often brightly colored as well.

Liquid nicotine comes in a variety of scents and candy flavors. Liquid nicotine has been sold in thousands of different flavors, including many flavors that appeal to children like “Cotton Candy” and “Grape Bubblegum” (see Appendix B). Research has shown that children and adolescents are more prone to be attracted to flavors that may be or appear to be sweet, increasing the likelihood that fruit and other sweet flavors will attract younger users.<sup>27</sup> Further, the compounds used to create many of the flavors for liquid nicotine are also used to flavor

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<sup>23</sup> King BA, Patel R, and SR Dube. Trend in awareness and use of electronic cigarettes among U.S. adults, 2010-2013. *Nicotine & Tobacco Research*. 19 Sept. 2014.

<http://ntr.oxfordjournals.org/content/early/2014/09/19/ntr.ntu191.full.pdf+html>.

<sup>24</sup> Tobacco use among middle and high school students – United States, 2011-2014. *Morbidity and Mortality Weekly Report*. Centers for Disease Control and Prevention. 17 April 2015. 64(14); 381-385.

<sup>25</sup> Garbutt JM, et al. Parental use of electronic cigarettes. *Academic Pediatrics*. 25 Aug. 2015.

<sup>26</sup> Ibid.

<sup>27</sup> De Graaf C and Zandstra EH. Sweetness intensity and pleasantness in children, adolescents, and adults. *Physiology and Behavior*. October 1999. 67(4); 512-20.

candy and soft drinks that appeal to children, such as 1-hexanol, which was detected in apple-flavored candy and all apple-flavored tobacco products tested in one study.<sup>28</sup>

In general, unintentional ingestions are highest among children under age five,<sup>29</sup> for the simple reason that mouthing is a normal developmental and learning tool for younger children.<sup>30</sup> Young children are also naturally curious to explore their environment, and understandably lack awareness of the consequences of such exploration. Young children with normal gross and fine motor development may have the ability to open a liquid nicotine container, but not to open it in a way that avoids spillage. In fact, many containers of liquid nicotine currently on the market can be easily opened even by young children. It is also widely known that children mimic adult behaviors, making children who see their parents use liquid nicotine potentially more likely to be interested in exploring it themselves. Therefore, when it comes to easily accessible, appealing, toxic substances such as liquid nicotine, a young child's expressions of normal development can put them at risk of exposure and serious harm.

Children are vulnerable not only to containers of liquid nicotine, but also to e-cigarette devices themselves. Calls to poison control centers include a sizable percentage of cases related to contact with the e-cigarette devices.<sup>31</sup> Children observe adults using and refilling e-cigarette devices and may mimic these behaviors as well. Many refillable e-cigarettes have reservoirs with an approximate capacity of 2 ml. Larger varieties can hold 4 ml or more of liquid nicotine. Especially when using highly concentrated liquid nicotine, these devices have a large enough capacity to hold a potentially lethal dose of nicotine for a small child if that child is able to gain access to a filled reservoir of liquid nicotine.

#### **D. Child-Resistant Packaging Paired with Warnings Protect Children**

It is well established that specially designed packaging can help to protect children from dangerous products. Child-resistant packaging, or “special packaging” as it is described under the Poison Prevention Packaging Act of 1970 (PPPA), is “...packaging that is designed or constructed to be significantly difficult for children under 5 years of age to open or obtain a toxic or harmful amount of the substance contained therein within a reasonable time and not difficult for normal adults to use properly, but does not mean packaging which all such children cannot open or obtain a toxic or harmful amount within a reasonable time.”<sup>32</sup>

As a result of the PPPA and other efforts, serious poisonings of young children overall have been at historically low levels; over the past 50 years, child poisoning deaths have decreased from 400

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<sup>28</sup> Brown J et al. Candy flavorings in tobacco. *New England Journal of Medicine*. 2014; 370: 2250-2252. [http://www.nejm.org/doi/full/10.1056/NEJMc1403015?query=featured\\_home](http://www.nejm.org/doi/full/10.1056/NEJMc1403015?query=featured_home).

<sup>29</sup> See "Poisonings," Protect the ones you love: Child injuries are preventable. Centers for Disease Control and Prevention. Accessed 17 August 2015. <http://www.cdc.gov/safecchild/NAP/background.html#cause>.

<sup>30</sup> Juberg DR, et al. An observational study of object mouthing behavior by young children. *Pediatrics*. 1 Jan. 2001. 107(1); 135-142. <http://pediatrics.aappublications.org/content/107/1/135.abstract>.

<sup>31</sup> Mowry JB et al. 2012 annual report of the American association of poison control centers' national poison data system (NPDS): 30<sup>th</sup> annual report. *Clinical Toxicology*. 2013. 51; 949-1229.

<sup>32</sup> Poison Prevention Packaging Act. 15 U.S.C. §1471(4).

to approximately 36 per year. As noted by the CPSC in its analysis of the PPPA, which establishes detailed requirements for special packaging:

*Special packaging saves lives. CPSC analyzed child fatality data for unintentional ingestions of oral prescription medicines during the 1964 through 1992 timeframe. The results of the analysis showed that the death rates for oral prescription medicines declined even after taking into account the changes in the consumption of the medications over time and the long-term decline in the overall unintentional death rate of children from all causes. The CPSC study showed that special packaging reduced the oral prescription medicine-related death rate by up to 1.4 deaths per million children under age 5. This represents a reduction in the rate of fatalities of up to 45 percent from levels that would have been projected in the absence of special packaging requirements, and equates to about 24 fewer child deaths annually. A similar study of the effectiveness of special packaging of aspirin estimated that special packaging reduced the aspirin-related mortality rate by 34 percent. This equates to about 90 fewer child deaths from aspirin during the 1973-1990 study period.*

*When combining the statistics for aspirin with those for prescription drugs, the staff of the CPSC estimates that special packaging saved the lives of more than 900 children since the requirements went into effect in the early 1970s. This estimate relates to aspirin and oral prescription medicines only and does not include additional lives that may have been saved by special packaging on other products.<sup>33</sup>*

History has shown that the adoption of child-resistant packaging is a very effective strategy for reducing the risk to children.<sup>34</sup> In contrast, warning labels have been shown to be on the whole only moderately effective on their own in preventing poisonings and other injuries.<sup>35</sup> Meta-analyses of warnings have indicated that consumers are more likely to comply with warnings for a product that is familiar, rather than unfamiliar, to the consumer.<sup>36</sup> Warning labels are generally helpful and needed to educate the public about poisoning risks, but warning labels should only supplement, and not substitute for, child-resistant packaging. Experience has taught us that manufacturers must “design out” the hazard. Putting dangerous products in child-resistant packaging, much like household cleaners and prescription and certain over-the-counter drugs, is a key design strategy to reduce the hazard to children.

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<sup>33</sup> Poison prevention packaging: A guide for healthcare professionals. Consumer Product Safety Commission. 2005. <https://www.cpsc.gov/PageFiles/113945/384.pdf>.

<sup>34</sup> Walton WW. An evaluation of the Poison Prevention Packaging Act. *Pediatrics*. 1982 Mar;69(3):363-70.

<sup>35</sup> Peden M et al. Eds. World report on child injury prevention. 2008. World Health Organization: Geneva.

<sup>36</sup> Argo JJ and KJ Main. Meta-analyses of the effectiveness of warning labels. *Journal of Public Policy & Marketing*. Fall 2004, 23(2); 193-208.

## II. FDA HAS CLEAR AUTHORITY UNDER THE TOBACCO CONTROL ACT TO REGULATE TOBACCO PRODUCTS TO PREVENT CHILD POISONING

The Family Smoking Prevention and Tobacco Control Act (herein referred to as the Tobacco Control Act),<sup>37</sup> signed into law in 2009, amended the Food, Drug, and Cosmetic Act (FDCA) to create clear authority for the FDA to regulate tobacco products for the purposes of protecting the public health. While the Tobacco Control Act gave the FDA immediate authority over cigarettes, smokeless tobacco, and roll-your-own tobacco, Congress left it for the FDA to deem through rulemaking any or all other types of tobacco products, including e-cigarettes and liquid nicotine, subject to the FDA's authority under the Tobacco Control Act. While our organizations applauded the long-awaited publication of the FDA's proposed rule last April to deem all tobacco products, including e-cigarettes and liquid nicotine, subject to the FDA's statutory authority, the final deeming rule has yet to be published.

### A. *FDA May Take Regulatory Action Appropriate for the Protection of Public Health*

As previously noted, liquid nicotine is extremely toxic and represents a significant public health hazard. Consequently, under the FDCA the FDA may take several forms of regulatory action with regard to tobacco products, including e-cigarettes and liquid nicotine, and components and parts, including liquid nicotine containers, in order to protect the public from the risk of nicotine poisoning.

#### (i) *Product Standards Under Section 907: Child-Resistant Packaging*

Under Section 907 of the FDCA, the FDA has clear authority to promulgate tobacco product standards appropriate for the protection of public health. Specifically, the statute states that a tobacco product standard issued under Section 907 includes "provisions respecting the construction, components, ingredients, additives, [and] constituents..." of tobacco products.<sup>38</sup> In the preamble to its proposed deeming rule, the FDA emphasizes this point, indicating that the agency could issue standards "regarding additives, constituents, or other components"<sup>39</sup> of tobacco products. As such, product standards could include child-resistant packaging (including devices to restrict the flow of liquid) and any other standards necessary for the protection of the public health.

For tobacco product standards, in making a determination of the appropriateness of the standard for the protection of the public health, the FDA must assess "the risks and benefits to the population as a whole, including users and nonusers of tobacco products..."<sup>40</sup> The use of child-resistant packaging on liquid nicotine containers would have no negative effect on users of e-cigarettes as long as child-resistant packaging standards ensure adult access to the consumer product (which the PPPA contemplates). In fact, such packaging could benefit adolescent and

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<sup>37</sup> Public Law 111-31.

<sup>38</sup> Food, Drug, and Cosmetic Act Sec. 907(a)(4)(B)(ii). 21 U.S.C. §387g(a)(4)(B)(ii).

<sup>39</sup> 79 Federal Register 23149.

<sup>40</sup> Food, Drug, and Cosmetic Act Sec. 907(a)(3)(B)(i)(I). 21 U.S.C. §387g(a)(3)(B)(i)(I).

adult users by preventing unintentional dermal contact with liquid nicotine, particularly if the packaging restricted the flow of liquid from the package. For non-users of these products, especially young children, child-resistant packaging on these products would provide substantial benefits by reducing the risk of unintentional poisoning.

*(ii) Restrictions on Sale and Distribution Under Section 906(d): Child-Resistant Packaging and Nicotine Exposure Warnings*

Under Section 906(d) of the FDCA, the FDA has the authority to require “restrictions on the sale and distribution of a tobacco product,” such as liquid nicotine. The FDA could use this authority to prohibit that sale and distribution of liquid nicotine without child-resistant packaging. This authority also includes the ability to prohibit the distribution and sale of tobacco products without appropriate nicotine exposure warnings given the high degree of risk these products pose especially to young children. Indeed, in its proposed deeming rule, the FDA invoked Section 906(d) as the authority for its proposed warning about the addictiveness of nicotine.<sup>41</sup>

Section 906(d)(1) specifies that the FDA may adopt a regulation if it finds that a sale and distribution restriction is “appropriate for the protection of the public health” ... “with respect to the risks and benefits to the population as a whole, including users and nonusers of the tobacco product...”<sup>42</sup> As previously demonstrated, liquid nicotine poisoning is a danger to both users (adolescents and adults who use e-cigarettes) and non-users (most importantly, young children) alike. Therefore, a restriction requiring nicotine exposure warnings would benefit both users and non-users by alerting both users and non-users (for example, child caregivers) to the health risks of dermal and oral exposure to liquid nicotine. In addition, such a restriction would have no foreseeable risk to non-users and would likely have a negligible impact on the usage behavior of users since such warnings would not directly discourage the use of the product as intended.

*(iii) Premarket Review Requirements Under Section 910*

Under Section 910 of the FDCA, the FDA has the authority through the premarket review process to prevent the entry of new tobacco products on the market unless the products have been shown to be appropriate for the protection of the public health, including the inclusion of child-resistant packaging. The premarket review process would also generally require that new tobacco products fully comply with the requirements of Section 906(d) as well as product standards established under Section 907 and would require that any labeling applied to these products, including labeling changes required through sales or marketing restrictions under Section 906(d), cannot be false or misleading.

A new tobacco product application submitted under section 910 would be required to include data on the “health risks” of the product, which could include data on the risk of nicotine poisoning, “a full statement of the components...and properties” of the product, which could include packaging technologies to reduce the risk of nicotine poisoning, and “the labeling

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<sup>41</sup> 79 Federal Register 23146.

<sup>42</sup> Food, Drug, and Cosmetic Act Sec. 906(d)(1). 21 U.S.C. §387f(d)(1).

proposed to be used” for the product, which could include warnings related to nicotine exposure.<sup>43</sup>

The FDA has clear authority under Section 910(c)(2)(A) to deny any application that does not effectively show that the product “would be appropriate for the protection of the public health” and the risk of child poisoning is an obvious and important consideration in this determination.

***B. No Other Federal Agency Has the Current Authority to Regulate Tobacco Products to Reduce the Risk of Child Poisoning***

It must be noted that not only does the FDA have clear authority to regulate e-cigarettes and liquid nicotine to reduce the risk of child poisoning, but the FDA is also the only federal agency with the current legal authority of regulating such products for this purpose. As mentioned previously, the CPSC has regulated special packaging (child-resistant packaging) under the PPPA for several decades.<sup>44</sup> However, tobacco and tobacco products are explicitly excluded from the definition of a “consumer product” under the Consumer Product Safety Act. Tobacco and tobacco products are also excluded from the definition of “hazardous substance” in the Federal Hazardous Substances Act (FHSA), which the PPPA references in its definition of “household substance.”<sup>45</sup> Because of this statutory language, and unless and until legislation creating some type of exception to these prohibitions were to be enacted, the CPSC is barred from taking action to apply special packaging to tobacco products like liquid nicotine.<sup>46</sup> Therefore, as the only agency with current jurisdiction, the FDA has a duty to use its regulatory authority to protect the public health from the poisoning hazards associated with e-cigarettes and liquid nicotine. Moreover, the FDA has broad enforcement authority to ensure compliance, including its authority to take action against adulterated or misbranded tobacco products under Sections 902 and 903 of the FDCA as amended, its authority to require registration of tobacco product manufacturers and reporting of their products under Section 905, and required records and reports on tobacco products under Section 909.

**III. FDA MUST TAKE URGENT ACTION TO REDUCE THE RISK OF CHILD POISONING RELATED TO TOBACCO PRODUCTS**

The FDA has been too slow to act on the issue of nicotine poisoning. Although it could have and should have, the proposed deeming rule, published on April 25, 2014, did not propose any actions to reduce the risk of nicotine poisoning to children, despite the FDA having the authority to take such actions in the deeming rule itself.<sup>47</sup> This failure occurred despite data being available to the agency that the problem was increasing. Earlier that month, on April 4, 2014, the FDA co-

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<sup>43</sup> Food, Drug, and Cosmetic Act Sec. 910(b)(1). 21 U.S.C. §387j(b)(1).

<sup>44</sup> The Poison Prevention Packaging Act. 15 U.S.C. §1471(4).

<sup>45</sup> Consumer Product Safety Act. 15 U.S.C. §2052(a)(5)(B).

<sup>46</sup> Federal Hazardous Substances Act. 15 U.S.C. §1261(f)(2).

<sup>47</sup> Just as the FDA determined, in the proposed deeming rule, that it has the authority to mandate minimum age and identification requirements (including vending machine requirements) and health warnings under Section 906(d)(1), it could have invoked that same authority to mandate child-resistant packaging and nicotine exposure warnings as components of the deeming rule.

authored an article published in the CDC Morbidity and Mortality Weekly Report (MMWR) that described the rising rates of calls to poison control centers related to e-cigarette and liquid nicotine exposures.<sup>48</sup> The publication of the ANPRM, the FDA's first significant action on this issue and its first public notice that it is actively considering rulemaking, did not occur until approximately 15 months after the publication of the MMWR. Moreover, in publishing an advance notice of proposed rulemaking, rather than proceeding directly to the publication of a proposed rule, the FDA has chosen to add an optional additional step in the regulatory process that our organizations are concerned will delay the ultimate promulgation of final, actionable rules to prevent child poisoning.

While 15 states have passed laws requiring some form of child-resistant packaging on liquid nicotine containers and other novel tobacco products, not all laws refer to the federal standards enforced by the CPSC and state enforcement of these laws may not be robust. In order to ensure that all children are protected from the dangers of liquid nicotine, a comprehensive federal standard must be established and enforced.

The undersigned organizations urge the FDA to quickly take four specific actions to reduce the risk of child poisoning from liquid nicotine:

**A. *FDA Should Publish a Proposed Rule As Soon As Possible Requiring Child-Resistant Packaging and Nicotine Exposure Warnings on Liquid Nicotine Containers***

Given the urgency of ensuring that liquid nicotine containers are sold in child-resistant packaging and that consumers are appropriately warned about the dangers of nicotine exposure, our organizations urge the FDA to work as quickly as possible to publish a proposed rule to institute these two policies. These policies should apply to any liquid nicotine container, which should be defined as a container holding a liquid solution containing nicotine in any concentration. This would not only include liquid nicotine used in e-cigarettes and similar devices, but also other liquid-based novel products such as nicotine drinks, nicotine gels, nicotine lotions, or nicotine inhalers that meet the definition of “tobacco product” under the FDCA.<sup>49</sup>

*(i) Child-Resistant Packaging*

Under its authority to issue product standards under Section 907 of the FDCA and its authority to impose sales and distribution restrictions under Section 906(d), the FDA should propose that all liquid nicotine containers be sold in child-resistant packaging.

Our organizations do not recommend that the FDA initially adopt novel standards for child resistance. Rather we recommend that the FDA initially adopt the effective existing standards established by the CPSC under the PPPA. The CPSC has long-standing and well-proven special packaging standards to reduce the risk of children accessing dangerous products. These standards

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<sup>48</sup> Notes from the field: Calls to poison centers for exposures to electronic cigarettes – United States, September 2010 – February 2010. *Morbidity and Mortality Weekly Report*. Centers for Disease Control and Prevention. 4 April 2014. 63(13); 292-293. <http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6313a4.htm>.

<sup>49</sup> Quick Nic. <https://quicknicmist.com>.

are described in the PPPA implementing regulations, in 16 CFR 1700.15. They do not proscribe specific product designs or child-resistant technologies, but rather require that products meet performance standards to ensure that they are sufficiently difficult for children to open. The standards require “child-resistant effectiveness of not less than 85 percent without a demonstration and not less than 80 percent after a demonstration of the proper means of opening such special packaging.”<sup>50</sup>

Manufacturers of these products are required to demonstrate that the products meet these performance standards by testing them in accordance with regulations outlined in 16 CFR 1700.20. The test generally gives panels of 50 children (aged 42-51 months) a span of 10 minutes to attempt to open a package. After five minutes, testers are required to demonstrate to the children how to open the package and give them another five minutes to do so, with a specific instruction that they may also use their teeth to try to open the package. A product is considered to have passed the test if 80% of the children are unable to open the package in the allotted time. The regulations also require that the products be tested by seniors to ensure that they are not too difficult for seniors to open them.

We recommend that any container that contains liquid nicotine and is clearly designed to be opened by the consumer be subject to the performance standards and testing described above. For products that contain liquid nicotine but are not designed to be opened by the user, such as pre-filled, sealed, and disposable e-cigarettes and cartridges, the CPSC testing regime would not be appropriate because it requires that tested packages be openable by adults. Rather, these sealed products should be held to a significantly higher standard. The FDA should ensure that it be virtually impossible for any such products to be opened or for children to come into contact with the liquid nicotine inside them, including by sucking on or piercing a seal on a cartridge.

The special packaging regulations under 16 CFR 1700.15 also require the restricted flow of liquids. Specifically, 1700.15(d) requires that the “flow of liquid is so restricted that not more than 2 milliliters of the contents can be obtained when the inverted, opened container is taken or squeezed once or when the container is otherwise activated once.” Liquid nicotine containers vary widely in terms of the rate of flow that can be achieved. Of particular concern are containers that include Pasteur pipettes (see Appendix C). For this type of product, once the pipette is removed from the container, the remainder of the liquid can flow out virtually unrestricted. Flow restricting devices can limit the amount of liquid that can emerge from a bottle in one squeeze, suck, or shake, and can help to prevent children from accessing the full contents of a container even if they are able to open it.<sup>51</sup> Flow restrictors have been an important strategy for children’s antipyretic/analgesics, and have been shown to be effective for preventing unintentional

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<sup>50</sup> Poison Prevention Packaging Act. 16 CFR §1700.15(b)(1).

<sup>51</sup> Lovegrove MC., et al. Efficacy of flow restrictors in limiting access of liquid medications by young children. *The Journal of Pediatrics*. 2013. 163(4); 1134-1139.

ingestions of substances by children, even when a child-resistant lid is not fully secured.<sup>52,53</sup> Further, the FDA's recently published final guidance on over-the-counter pediatric oral liquid drug products acknowledges the FDA's previous work on this topic and importance of flow restrictors on liquid drugs to ensure that children are safe.<sup>54</sup>

We therefore urge the FDA to require effective flow restrictors on liquid nicotine containers. However, the 2 ml standard for flow restrictors under the PPPA is potentially problematic in the case of liquid nicotine, since 2 ml is well within the range of a theoretical lethal dose of liquid nicotine for a 1-year-old child at various nicotine concentrations (see Table 1). We urge the FDA to carefully consider requiring a more stringent standard such as requiring flow to be restricted to no more than one drop per activation. This should be carefully balanced with the risk that a parent or caregiver would remove or otherwise disable a flow restrictor to increase the rate of flow.

Given the CPSC's experience in administering the PPPA, and given that the FDA and the CPSC have worked together to prevent child poisonings from prescription drug bottles, we urge the FDA to consult with the CPSC as it undertakes implementation of child-resistant packaging (that is at least as protective as the special packaging defined by the PPPA) for liquid nicotine containers. To inform the establishment of product standards for the protection of public health, the Tobacco Control Act allows the FDA to "consult with other Federal agencies concerned with standard setting and other national or internationally-recognized standard setting entities," which would include child-resistant packaging standards administered by the CPSC under the PPPA.<sup>55</sup>

We urge that a child-resistance requirement be enforced as soon as possible after the publication of the final rule, especially given that the rule would not affect the timeline for the production of the liquid nicotine itself and the urgency of the public health threat presented by liquid nicotine poisoning. Section 907(d)(2) of the FDCA generally requires that no final product standard "take effect before 1 year after the date of its publication unless the Secretary determines that an earlier effective date is necessary for the protection of the public health." Since containers that already meet CPSC's requirements for special packaging are readily available for purchase and use by manufacturers, the FDA should establish an effective date of no longer than six months after publication of a final rule. The public health threat is immediate, since one child has already died, and a solution is well-known.

#### *(ii) Warning Labels*

In the ANPRM, the FDA seeks comment on whether warning labels can be effective in combatting the poisoning hazards posed by liquid nicotine. Warning labels are helpful and

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<sup>52</sup> Ibid.

<sup>53</sup> "How safe is your baby's medicine bottle?" *Consumer Reports*. December 2013.

<http://www.consumerreports.org/cro/2013/12/flow-restrictors-to-prevent-accidental-acetaminophen-overdoses/index.htm>.

<sup>54</sup> Over-the-counter pediatric oral liquid drug products containing acetaminophen: Guidance for industry. Food and Drug Administration. August 2015. <http://www.fda.gov/ucm/groups/fdagov-public/@fdagov-drugs-gen/documents/document/ucm417568.pdf>.

<sup>55</sup> Food, Drug, and Cosmetic Act Sec. 907(a)(6)(B). 21 U.S.C. §387g(a)(6)(B).

needed to educate the public about the lethality of liquid nicotine and the need to keep these products out of reach of children, but warning labels should only supplement, and not substitute for, child-resistant packaging. We strongly urge the FDA to require child-resistant packaging, along with warnings, on liquid nicotine containers and not to rely on warnings alone to address this hazard.

Because of the unique risk that liquid nicotine poses to children, it is essential that a nicotine exposure warning specifically highlight the risk of harm to children and utilize tight, concise language to maximize effectiveness.<sup>56</sup> “Keep out of Reach of Children” is a common and familiar warning placed on many consumer products that pose various levels of risk to children. In our view, such a warning by itself would be insufficient to adequately convey the seriousness of the risk. Any nicotine exposure warning should specifically address that the product is highly poisonous and that exposure carries the risk of injury and death. Research has shown that warnings are more effective when they mention specific hazards.<sup>57</sup> A label should also warn about all of the known routes of absorption of liquid nicotine (oral, dermal, etc).

Finally, we recommend that nicotine exposure warning labels be required to list the toll-free number for Poison Help, the national poison helpline administered by the American Association of Poison Control Centers (1-800-222-1222). This number should be listed prominently on the label so that a caller can be routed to a geographically-appropriate specialist that can assess an exposure and recommend a course of action, which may include seeking urgent medical attention.

The FDA must carefully balance the completeness of information required in any nicotine exposure warning with the risk that the warning could become too long to be effective. Liquid nicotine containers are often small in size, so care must be taken to ensure that the font size of any required warnings remains large enough to be noticed and read.

***B. FDA Should Quickly Publish a Final Rule to Deem All Tobacco Products Subject to FDA’s Authority under the Tobacco Control Act***

The administration has yet to publish a final rule expanding its jurisdiction to include all types of tobacco products, including e-cigarettes and liquid nicotine. It has been well over four years since the FDA first informed the public of its intent to extend its authorities under the Tobacco Control Act to all tobacco products.<sup>58</sup> It has also been well over a year since the FDA published its proposed deeming rule to so expand its authorities. The administration has already missed one self-imposed deadline for the publication of a final deeming rule. It is absolutely essential that the administration finalize this rulemaking urgently. However, the issuance of a proposed rule

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<sup>56</sup> Testing of health warning messages and health information messages for tobacco product – part 1 of 5: Introduction and executive summary. Decima Research. June 2009. <http://www.tobaccolabels.ca/wp/wp-content/uploads/2013/12/Canada-2009-Testing-of-Health-Warning-Messages-and-Health-Information-Messages-for-Tobacco-Products-Government-Report.pdf>.

<sup>57</sup> Langlois JA, et al. The impact of specific toy warning labels. *JAMA*. 1991 Jun 5;265(21):2848-50.

<sup>58</sup> Regulation of e-cigarettes and other tobacco products. Stakeholder Letter. April 25, 2011. <http://www.fda.gov/NewsEvents/PublicHealthFocus/ucm252360.htm>.

mandating child-resistant packaging and appropriate warnings need not await a final deeming rule.

***C. FDA Should Plan to Utilize Its Premarket Review Authorities to Ensure that Products that Pose a Poisoning Risk Have Child-Resistant Packaging and Carry Nicotine Exposure Warnings***

If the FDA determines that it would be appropriate for the protection of public health to approve under Section 910 of the FDCA the marketing of any liquid nicotine products sold in an openable container, we would urge the FDA not approve any such application unless the product would be sold in a child-resistant container and bear nicotine exposure warnings.

After the publication of the final deeming rule, we would urge the FDA to quickly publish guidance for manufacturers on how to address nicotine poisoning prevention—including at a minimum through child-resistant packaging and nicotine exposure warnings—in the development of new tobacco product applications.

***D. FDA Should Not Accord a Lengthy Compliance Grace Period to Any Newly Deemed Liquid Nicotine Products Not Sold in Child-Resistant Packaging***

We are strongly supportive of the FDA's proposal in the deeming rule to use the premarket review process to prevent harmful tobacco products from reaching the market and as a framework for the FDA's oversight of novel tobacco products and their components. However, the proposed deeming rule suggested offering newly deemed tobacco products such as liquid nicotine a 24-month compliance period during which the FDA would not take action against these products that would otherwise be illegal if not (1) introduced into the market before February 15, 2007, (2) substantially equivalent to a product introduced into the market before February 15, 2007, or (3) marketed in accordance with a premarket order under Section 910 of the FDCA.

We believe the inclusion of a two-year enforcement grace period for newly deemed tobacco products to be misguided and inappropriate for the protection of public health, especially concerning liquid nicotine. In comments on the proposed deeming rule, many of our organizations requested that the FDA shorten the overall length of the enforcement grace period for newly deemed tobacco products to a year after the date of publication of the final deeming rule.

Given the poisoning threat caused by liquid nicotine and the fact that containers meeting CPSC's existing special packaging requirements are readily available on the market for purchase by manufacturers, we believe it inappropriate to give liquid nicotine products not sold in child-resistant packaging a grace period even as long as a year. Newly deemed tobacco products not packaged in accordance with CPSC's existing special packaging requirements should not be offered a grace period longer than six months from the effective date of the final deeming rule.

#### **IV. FDA SHOULD ALSO CONSIDER OTHER MEASURES TO REDUCE CHILD POISONING RISK RELATED TO TOBACCO PRODUCTS**

As mentioned above, we urge the FDA to quickly address, through rulemaking and other means, child-resistant packaging and nicotine exposure warnings for e-cigarettes and other liquid nicotine containers. While there are other important aspects of child nicotine poisoning prevention to be addressed and considered, the FDA should not allow the consideration of these issues to delay urgent action on the above recommended actions regarding packaging and warnings.

Nevertheless, the FDA remains the only federal agency with the authority to regulate tobacco products to prevent child poisoning. After it has implemented child-resistant packaging standards and nicotine exposure warnings on an expedited basis as described herein, it is essential that the FDA address this issue in a comprehensive manner, considering the full range of tobacco products, the full range strategies to reduce poisoning risk, and the full range of the FDA's authorities and resources. Many of these issues may be most appropriately addressed in the context of premarket review of new tobacco products.

##### ***A. FDA Should Conduct a Comprehensive Assessment of Poisoning Risks Posed by the Various Types of Tobacco Products***

The FDA should conduct a comprehensive assessment of the child poisoning risks posed by all types of tobacco products. Given the increased development and use of novel tobacco products and the lack of extensive research concerning the risks of these products and their corresponding components to the public health, a thorough and comprehensive scientific evaluation of these products and their effects on both youth and the public at large is needed.<sup>59</sup> This research will be essential in establishing a robust regulatory framework for the evaluation of new and existing tobacco products to minimize risks and ensure that all proper safeguards are applied to these products, ideally before their entrance into the market. Non-combustible products that are designed to be placed in the mouth, such as dissolvables and other smokeless tobacco products, are concerning from a child safety perspective and the FDA should carefully consider strategies to reduce the risks associated with these products. The FDA should also assess the frequency of and danger posed by ocular exposures<sup>60</sup> of liquid nicotine, including whether they are likely to cause nicotine toxicity or damage to the eye, and take appropriate regulatory responses if necessary.

It is vitally important that the FDA remain vigilant in monitoring emerging trends in child exposures and harms caused by tobacco products, both by collecting and analyzing adverse event reports and by ensuring that it has real-time access to complete poison control center data. The FDA should also conduct a careful assessment of the impacts of any regulatory actions it takes with respect to child-resistant packaging and nicotine exposure warning to ensure their

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<sup>59</sup> Connolly CH et al. Unintentional child poisonings through ingestion of conventional and novel tobacco products. *Pediatrics*. May 2010. 125(5); 896-899.

<sup>60</sup> Chatham-Stephen K, et al. Calls to Poison Centers for Exposures to Electronic Cigarettes – United States, September 2010 – February 2014. Centers for Disease Control and Prevention. *MMWR* April 4, 2014, Vol. 63, No. 10.

effectiveness. Such an assessment should consider whether changes should be made to make any required standards stricter if necessary to protect the public health.

### ***B. FDA Should Consider the Use of Graphics in Warning Labels***

The use of graphics<sup>61</sup> to convey poisoning risk is an important consideration, particularly since graphics have the potential to directly reach children who cannot read and parents and caregivers with low literacy or limited English proficiency. Graphics must be carefully analyzed to predict their impact not only on caregivers but also on children. For instance, while a “skull-and-crossbones” symbol may be effective at conveying poisoning risk to an adult, a child might associate such a symbol with pirates, thereby potentially increasing the child’s attraction to the product.<sup>62</sup> One study found the “Mr. Yuk” sticker to be more effective than the “skull-and-crossbones” symbol in reducing child interest.<sup>63</sup> However, use of the “Mr. Yuk” sticker was discontinued by some as research indicated that children could be actually attracted to the stickers featuring a bright green, frowning face, and that the effectiveness of the warnings depended upon the personality and developmental level of the child.<sup>64,65</sup> Similarly, the colors of graphics and the text for warning labels must also be analyzed for effectiveness among children. For example, certain combinations of symbol and background colors have been shown to be more effective than other comparable color options and text highlighting has been shown to be more effective than warnings without highlighting.<sup>66,67</sup>

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<sup>61</sup> In developing appropriate graphics as part of warning labels, FDA should give due consideration to the constitutional analysis of graphic health warnings on tobacco products in prior federal court decisions, but there is little doubt that simple graphic representations conveying a poisoning danger to children would survive First Amendment challenge. *See e.g., Discount Tobacco City & Lottery v. United States of America*, 674 F.3d 509 (6<sup>th</sup> Cir. 2012) (upholding statutory requirement of color graphics on cigarette packages depicting the negative health consequences of smoking against First Amendment challenge); *R.J. Reynolds Tobacco Co. v. FDA*, 696 F.3d 1205 (D.C. Cir. 2012) (striking down FDA regulation mandating specific graphic warnings as violation of First Amendment), *overruled in part*, *American Meat Institute v. U.S. Dept. of Agriculture*, 760 F.3d 18 (D.C. Cir. 2014) (*en banc*) (holding governmental interests other than preventing deception may be invoked to apply lenient standard of review of government mandate for disclosure of purely factual information and overruling *R.J. Reynolds* to the extent it holds the contrary).

<sup>62</sup> Fisher K. “Yeech! It’s mr. yuk, he’s poison.” *Pittsburgh Post-Gazette*. 25 June 1973.

<https://news.google.com/newspapers?nid=1129&dat=19730625&id=b59RAAAIBAJ&sjid=LG0DAAAIBAJ&pg=2619,3394357&hl=en>.

<sup>63</sup> McCarrick C and T Ziaukas. Still scary after all these years: Mr. yuk nears 40. *Western Pennsylvania History*. Fall 2009. <http://journals.psu.edu/wph/article/viewFile/7926/7699>.

<sup>64</sup> “IPC Stops Offering Mr. Yuk Stickers,” <https://illinoispoisoncenter.org/mr.yuk>.

<sup>65</sup> “Mr. Yuk, a Retired Poison Prevention Icon,” <https://www.nnepc.org/med-safety/mr-yuk-a-retired-poison-prevention-icon>.

<sup>66</sup> Chen CF and KC Huang. Characteristics of warning labels for drug containers and their effects on perceived hazardousness. *Safety Science*. 2015. 78; 149-154.

<sup>67</sup> McDougald BR and MS Wogalter. Facilitating pictorial comprehension with color highlighting. *Applied Ergonomics*. September 2014. 45(5); 1285-1290.

### ***C. FDA Should Consider Public Awareness Activities***

Since liquid nicotine and other novel tobacco products are relatively new additions to the market, the public is likely largely unaware of the dangers these products pose to young children. The FDA should consider actively promoting a greater public understanding of these risks.

### ***D. FDA Should Consider Restrictions on the Use of Packaging Attractive to Children***

The FDA should consider regulating liquid nicotine containers to make them less attractive to children. Specifically, the FDA should conduct an investigation and open a docket to consider (1) prohibiting the use of bright colors on liquid nicotine containers, (2) prohibiting the use of bright colorings in the liquid itself, (3) prohibiting the use of pictures of fruit and other food products on liquid nicotine containers, and (4) requiring black and white, text-only packaging for liquid nicotine containers.

In considering these strategies, the FDA should be cautious about previous federal court rulings related to tobacco marketing and the First Amendment.<sup>68</sup> For instance, to avoid potential challenge to restrictions on a manufacturer's ability to use color and graphics in its labeling, the FDA could consider applying certain restrictions only to the immediate liquid nicotine container and not to exterior retail packaging designed to be discarded before use.

### ***E. FDA Should Prohibit the Use of Flavors***

As noted in the comments filed by many of the undersigned organizations on the proposed deeming rule,<sup>69</sup> since flavorings/scents are particularly attractive to children and the flavorings/scents used in liquid nicotine are often similar or identical to ones used in children's food products and candy, the FDA should prohibit characterizing flavors in e-cigarettes and other liquid nicotine products. Such a prohibition would not only reduce the attractiveness of these products to older children and teens interested in using the products, but it would also reduce the risk that young children would be attracted to and attempt to ingest liquid nicotine.

### ***F. FDA Should Consider Limiting Liquid Nicotine Quantity and Concentration***

As with most toxins, the severity of nicotine poisoning is highly dose dependent. For instance, halving the amount of nicotine exposure roughly halves the magnitude of negative effects. The FDA should consider mechanisms other than child-resistant packaging that may reduce the amount of nicotine a child might come into contact with in case of unintentional exposure. The FDA could consider, therefore, instituting a maximum volume for an individual container of liquid nicotine, a maximum concentration of nicotine in a liquid nicotine solution, or a maximum total amount of nicotine by mass in an individual container. The FDA, however, should be

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<sup>68</sup> See *Discount Tobacco City & Lottery, Inc. et al. v. United States*, *supra* at 548..

<sup>69</sup> Comments filed by American Academy of Family Physicians, American Academy of Pediatrics, et al., in Docket No. FDA-2014-N-0189, RIN 0910-AG30, Proposed Rule on Deeming Tobacco Products to be Subject to the Federal Food, Drug and Cosmetic Act, as Amended by the Tobacco Control Act; Regulations on the Sale and Distribution of Tobacco Products and Required Warning Statements for Tobacco Products, August 8, 2014, at 46-49.

careful in considering adjustments to liquid nicotine concentration in particular as such a policy change may have public health implications beyond nicotine poisoning since varying nicotine levels would likely result in changes in user behavior.

***G. FDA Should Consider Protecting Children against Inhalation Exposure***

These comments primarily focus on the danger that children may be exposed directly to liquid nicotine, either through oral or dermal contact. However, we urge the FDA to investigate the possibility that young children may be harmed by using e-cigarettes, nicotine inhalers, or other nicotine delivery systems as they are intended to be used by adults: through inhalation of aerosolized liquid nicotine. Many e-cigarettes activate automatically when the user places the product in the mouth and breathes in. Young children are likely to mimic adult usage behavior and attempt to use e-cigarettes as adults do. The FDA should consider the potential for this type of usage by young children to cause toxicity or other negative health effects, especially since inhalation exposures accounted for 16.8% of calls to poison centers between September 2010 and February 2014.<sup>70</sup> Technologies to prevent the activation of these products by young children should be considered.

***H. FDA Should Consider Protecting Children from Refillable Devices***

E-cigarettes or similar devices that can be refilled with liquid nicotine by the user (as opposed to disposable e-cigarettes or those made to accept sealed and pre-filled disposable cartridges) can pose a child poisoning risk if a child gains access to the liquid nicotine in a filled device. To the extent that the FDA can regulate these devices, our organizations would urge the FDA to consider applying similar or identical child-resistant packaging requirements to these devices to ensure that these devices are sufficiently difficult for children to open.

## **CONCLUSION**

Our groups thank you for the opportunity to comment on this urgent public health matter. We strongly urge the FDA to take immediate action to address this important issue to prevent further harm to children. Please do not hesitate to reach out to our organizations if you have any questions about these comments.

Sincerely,

Academic Pediatric Association  
Action on Smoking & Health  
American Academy of Ophthalmology  
American Academy of Oral and Maxillofacial Pathology (AAOMP)  
American Academy of Family Physicians  
American Academy of Otolaryngology – Head and Neck Surgery  
American Academy of Pediatrics

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<sup>70</sup> Chatham-Stephens K, et al. Calls to Poison Centers for Exposures to Electronic Cigarettes – United States September 2010- February 2014. CDC MMWR: April 4, 2014, Vol. 63, No. 13.

American Association for Pediatric Ophthalmology and Strabismus  
American Association for Respiratory Care  
American Cancer Society Cancer Action Network  
American Congress of Obstetricians and Gynecologists  
American Heart Association  
American Lung Association  
American Pediatric Society  
American Public Health Association  
American School Health Association  
American Society of Addiction Medicine  
American Thoracic Society  
Americans for Nonsmokers' Rights  
Association of Maternal & Child Health Programs  
Association of Medical School Pediatric Department Chairs  
Association of Women's Health, Obstetric and Neonatal Nurses  
Campaign for Tobacco-Free Kids  
Community Anti-Drug Coalitions of America  
Consumer Federation of America  
First Focus Campaign for Children  
International Association for the Study of Lung Cancer  
Kids in Danger  
Lung Cancer Alliance  
March of Dimes  
National Association of County & City Health Officials  
National Association of Pediatric Nurse Practitioners  
National Center for Health Research  
National Latino Alliance for Health Equity  
National Native Network  
National Physicians Alliance  
Pediatric Policy Council  
Public Citizen  
Society for Pediatric Research  
Society for Public Health Education  
Society for Research on Nicotine and Tobacco  
The Society of Thoracic Surgeons  
Tobacco Control Legal Consortium  
U.S. PIRG

## APPENDIX A: USE OF IMAGES FAMILIAR AND APPEALING TO CHILDREN



Gummy Bears label design and flavoring.  
<http://www.affordablevapor.com/gummy-bears-e-liquid.html>.



Liquid nicotine container using trademarked image of a popular child food product.  
<http://bestejiceusa.com/smr-product/kaptain-krunch-peanut-butter/>.

## APPENDIX B: USE OF FLAVORS FAMILIAR AND APPEALING TO CHILDREN



Cotton Candy label design and flavoring.

<https://vaporhq.com/cotton-candy-e-liquid>.



Grape Bubblegum label design and flavoring.

<https://www.hookah-shisha.com/p-18106-cali-vape-grape-bubble-gum-e-liquid-18mg.html>



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masterpiecesmokeshop 'New ELiquid Alert' Swedish fish in a bottle. #fisheliquid 30ml bottles in 4mg 80VG/20PG, a perfect blend for clouds and flavor. #swedishfish #brooklyn #bushwick #masterpiece #clouds #comevape #driplife #driplyfe #ecig #eliquid #ejuice #flavorfordays #greenpoint #happyvaping #juicemeup #newjuice #nycvaper #newyorkcity #shoplocal #tasty #vape #vapor #vapeon #vapebar #premiumeliquid



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Master Piece Smoke Shop Instagram post, 8/10/15.

<https://instagram.com/p/6NeySWRFzS/>

#### APPENDIX C: LIQUID NICOTINE CONTAINER WITH NO FLOW RESTRICTION



Pasteur pipette-style bottle design with unrestricted lid.

